Oncology
and Radiotherapy©
18(7) 2024: 001-008 • RESEARCH ARTICLE

Robotic multi-visceral resection for locally-advanced rectal cancer: Initial experiences

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ABSTRACT

Background: Locally advanced rectal cancers (10%-20%) can present with infiltration into adjacent viscera. R0 resections remain the key factor for better survival. Traditionally these cases have been managed with open surgery. There are some limitations of laparoscopic surgery in these cases, which can potentially be overcome by robotic surgery.

Objectives: To determine the feasibility and outcome results of robotic multi-visceral resection of stage T4 rectal carcinoma.

Methods: Consecutive patients having locally advanced carcinoma of rectum, which undergone robotic multi-visceral resections as the primary treatment between 2015-2018 were included, through our database which was maintained prospectively. All perioperative and intraoperative parameters were analyzed. Patient demographics, co-morbidities, preoperative imaging, endoscopic findings, operative data, histopathology results, postoperative hospital course and procedure related postoperative adverse events were noted and analyzed.

Results: 21 patients with the diagnosis of non-metastatic locally advanced rectal cancers were operated with Robotic Si/X platform. The median body mass index was 28.5 kg/m^2 (range 21-42). The mean blood loss during operation was 20 ml (range 5-200), and the mean duration of surgery was 280 min (range 240-430). The median hospital stay after operation was 6 days (range 4 days-25 days). On postoperative histopathology, R0 Resection rate was 90.5% (19/21).

Conclusions: The robotic multi-visceral en-bloc resection of stage T4 rectal carcinoma is technically feasible and oncologically safe. Advanced technical skills, accurate radiological staging and careful patient selection can allow the extension of minimal access surgery to this challenging group of patients.

Keywords: T4 rectal cancers, en-bloc resection, multi-visceral resection, locally advanced rectal carcinoma, robotic resection

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Word count: 3691 **Tables:** 03 **Figures:** 05 **References:** 28

Received: 20 July, 2024, Manuscript No. OAR-24-142537
Editor Assigned: 21 July, 2024, Pre-QC No. OAR-24-142537(PQ)
Reviewed: 04 August, 2024, QC No. OAR-24-142537(Q)
Revised: 11 August, 2024, Manuscript No. OAR-24-142537(R)
Published: 18 August, 2024, Invoice No. J-142537

INTRODUCTION

Annually, there are 14000 new rectal carcinoma diagnosed in the UK and nearly half a million cases globally, and about 10%-20% are locally-advanced with invasion into adjacent viscera at presentation [1]. Intraoperatively, it is difficult to differentiate whether the adhesions between the tumor and adjacent viscera is due to malignant infiltration or desmoplasia. To achieve R0 resection, the standard practice is to perform en-bloc resection [2]. Nonetheless, resection of any locally advanced rectal carcinoma is technically difficult, which is associated with higher treatment failure rates and significant morbidity. This can be partially avoided by input from a well-coordinated multidisciplinary team, including surgeons, radiologist, pathologist, radiation and medical oncologists. The surgical aim in these patients is a complete resection of the tumor and rectum en-bloc with any involved viscera (R0 Resection) with preservation of quality of life.

An open procedure has been mostly used in vast majority of cases. The laparoscopic rectal surgery for rectal carcinoma is developed into a safe and effective treatment option. The laparoscopic rectal resection with total meso-rectum i.e. Total Mesorectal Excision (TME) is matching open resection in terms of quality of surgical specimen (i.e. resection margin) and long-term oncologic outcomes; however, it is technically demanding and still not established as the gold standard surgical procedure for rectal carcinoma [3-5]. The technical difficulties are attributed to the narrow anatomical space of the lower pelvis, restricted movements of the rigid laparoscopic instruments, obesity and bulky tumors [5-7]. Due to these technical difficulties, for locally advanced rectal carcinoma, laparoscopic surgery may result in incomplete resection and incomplete TME [8].

Robotic platforms (da Vinci® Si/X/Xi, Intuitive Surgical, California, USA) offer advantages in overcoming some of these technical difficulties and allow precise dissection in the narrow pelvis through motion scaling and intuitive manipulation, high-definition three-dimensional images (with up to 10x magnification) from a steady camera, endowrist instruments, and stable traction provided by the robotic arms [4-9]. With these potential benefits, robotic rectal surgeons have reported oncologic outcomes equivalent to laparoscopic surgery, and improved outcome in difficult clinical situations like obesity, male sex, post chemoradiotherapy, and cancers of the lower 2/3 of the rectum [5, 10-12].

Our unit has been performing Robotic colorectal surgery for the last 7 years and more than 500 colorectal cancer resections have been performed. As experience grew we have attempted robotic en-bloc resection of locally advanced rectal carcinoma, which we are presenting in this study. Our primary end-point was to assess the feasibility and oncological safety. The secondary end points included were operative duration, amount of blood loss, hospital course of stay and postoperative adverse events. To our knowledge this is one of the first reports looking at the outcomes of robotic assisted en-bloc resection of stage T4 rectal carcinomas.

METHODS

This study was conducted at the Queen Alexandra Hospital, Portsmouth, UK, from June 2015 to July 2018. The patients were included from an ethics approved prospective database kept at an associated teaching hospital for mandatory national audit.

All patients who underwent total robotic resection of stage T4 rectal cancers en-bloc with involved adjacent visceras were eligible for inclusion and enrolled in the study. The multi-visceral, en-bloc resection was performed on the basis of radiological or intraoperative indication of adjacent visceral invasion. The exclusion criteria included recurrent cancers, incomplete resection, resection in separate pieces, emergency resection, and patients receiving palliative treatment. Written, informed consent was obtained and patients were counseled about their overall physical status, disease condition, the potential risks and benefits of the operation, and other management options.

Preoperative workup

Preoperative work-up included rectal examination, endoanal ultrasound, pelvic Magnetic Resonance Imaging (MRI) and a staging Computed Tomography Scan (CT Scan) of chest, abdomen and pelvis. In some cases, Positron Emission Tomography-Computed Tomography (PET-CT) was also performed to rule out occult metastasis. All patients were discussed in a complex cancer Multidisciplinary Team (MDT) and planning X-ray meeting before surgery. Urological and gynecological advice was sought in relevant cases. The decision of neoadjuvant treatment was made after the MDT discussion. Tumors at a favorable location (upper rectum), anteriorly-based with uterine or peritoneal reflection involvement without the presence of large vessel Extramural Venous Invasion (EMVI) and good probability of R0 were directly scheduled for surgery. Others received neoadjuvant chemo radiotherapy with a view to downstage. Surgery in such patients was scheduled at 10 weeks-12 weeks post-chemo radiotherapy. All patients received mechanical bowel preparation with two sachets of picolax.

Operative procedure

Surgery was carried out using Da Vinci Si and X systems (Intuitive Surgical California, USA). A standardized technique was used, with single docking from the left hip. All patients were operated in modified lithotomy position with 10° Trendelenburg and 20° right tilt. Port placement for Si system is shown in figure 1. These included 4- mm 8-mm DaVinci ports at the right upper and lower, and left upper and lower abdomen and another 12 mm port laterally on right side (used as the assistant port for Si system). With the X system all robotic ports were placed on a straight line (Figure 2).

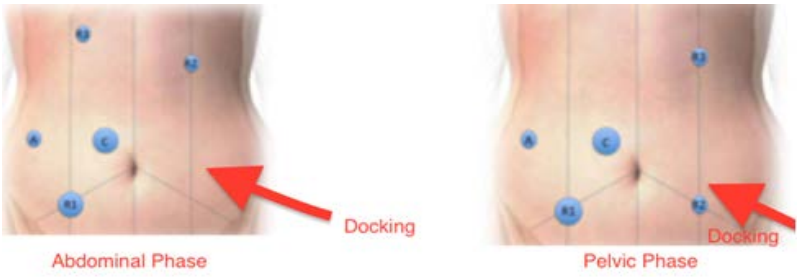

Fig. 1. Port placement for LAR with Si system

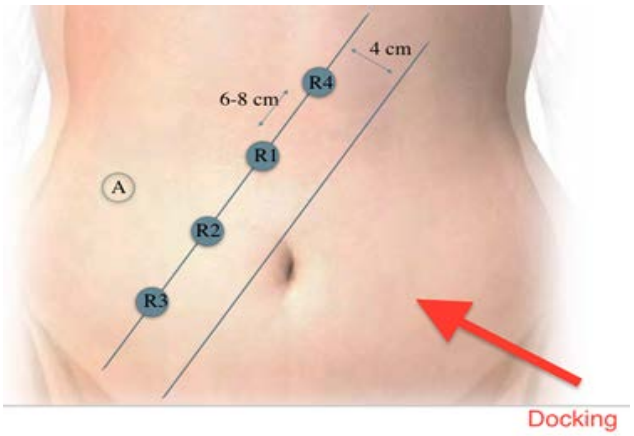

Fig. 2. Port placement for LAR with X system

After opening the retroperitoneal space at the sacral promontory, dissection continued in the midline to identify the inferior mesenteric artery, which was divided at its origin. The inferior mesenteric vein was divided below the inferior pancreatic border. We routinely mobilized splenic flexure to facilitate a tension-free anastomosis in the pelvis. The pelvic dissection was performed according to the TME principles. Any densely adherent adjacent viscera were included in the resection. Finally, resection of the cancerous segment was done via endoscopic stapling or inter-sphincteric resection, with restoration of bowel continuity with intracorporeal double stapling. A covering loop ileostomy was carried out in patients who had restorative anterior resection. Depending on the pattern of organ involvement, we extend our surgical resections beyond the normal anatomical planes. The adherent visceras were completely resected in an en-bloc fashion (Figure 3 and 4). Working together with the urologists on a dual console platform was very helpful in some of these challenging cases.

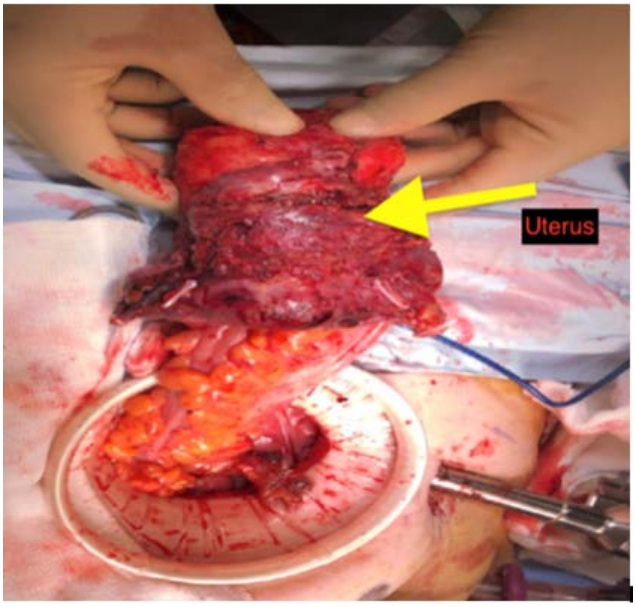

Fig. 3. Robotic anterior resection with en-bloc hysterectomy for locally advanced rectal cancer

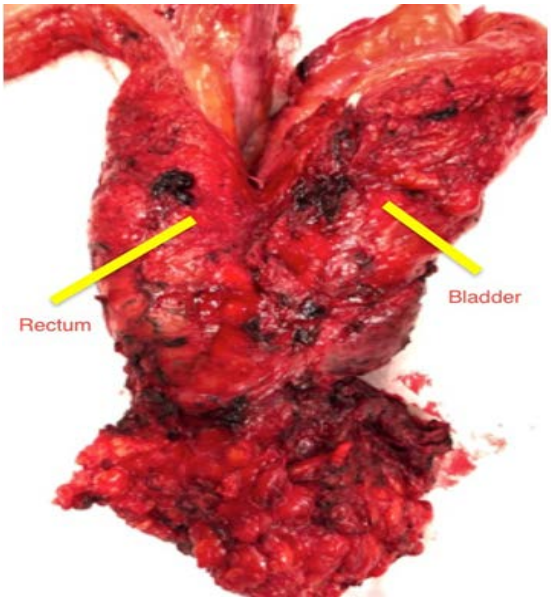

Fig. 4. Total pelvic clearance for T4 rectal cancer

T4 rectal cancer invading the bladder trigone received an exenterative procedure (total pelvic exenteration). Pararectal spaces were created on both sides after mobilizing and medializing ureters. Subsequently the bladder was mobilized from anterior abdominal wall and space of Retzius was dissected and connected with paravesical spaces. Puboprostatic ligament was then divided and the dorsal veins were suture ligated and divided followed by the division of the urethra. The ureters were divided distally and a bladder reconstruction was done with an ileal conduit. In women, tumors that involved the uterus/cervix we performed a posterior pelvic exenteration (rectum, uterus and partial vagina) with the robotic platform.

Postoperative care

All patients received adjuvant chemotherapy 6 weeks-8 weeks after rectal resection. In cases of diverting stoma, restoration of bowel continuity was completed after adjuvant chemotherapy. The procedure related postoperative adverse events that occurred within 90 days were recorded.

Outcome measures and statistical analysis

A prospective database was maintained for the evaluation of outcomes, both clinical and oncological. Our primary outcome endpoint was to assess the oncological safety and technical feasibility assessed by Circumferential Resection Margin (CRM) involvement and conversions to open procedure. The secondary endpoints were operative duration, amount of blood loss, hospital course of stay and procedure related postoperative adverse events. The histology of adjacent resected viscera was reviewed and cross-referenced with operative notes. Other secondary outcome variables were patient's survival, disease-free survival and recurrence; all obtained from cancer clinic surveillance records. Other variables noted and analyzed included patient demographics, comorbidities, colonoscopy findings and preoperative imaging (CT, PET, MRI). International Busniness Machines (IBM) SPSS Statistics software (*vs.* 23) was used for statistical analysis. Categorical variables data are presented as frequencies and percentages, while median (range) or mean (standard deviation) was used to assess continuous variables. Inferential statistics were calculated using the chi-square and t-test, and a p-value of <0.05 was considered significant.

RESULTS

Thirty-one patients were enrolled in this study having stage T4 rectal carcinoma invading adjacent viscera. Six of them had metastatic disease at presentation and were managed in a palliative setting. Two patients had a laparoscopic resection and 2 patients had an open procedure based on the operating surgeons' preference, and were excluded from the final analysis.

Twenty-one patients remained in the study for final analysis; thirteen (62%) of them were females, with a mean age of 74 years. Patient demographics are shown in table 1. Most patients were overweight, with a median body mass index of 28.5 kg/m^2. Fifty-seven percent of tumors were located in the lower two-thirds of rectum. Preoperative radiotherapy was used in 10 patients for down staging (7 long-courses, 3 short-courses). The involved visceras that were resected en-bloc included small bowel, urinary bladder, ovaries, uterus, vagina, seminal vesicles and prostate. Permanent stoma was made in 7 patients (Table 2).

Tab. 1. Physical and Radiological characteristics of Tref and Markus chamber

Characteristics	Patients (n=21)
Age (year), Median (range)	74 (40-82)
Sex, n (%)	
Male	8 (38)
Female	13 (62)
ody mass index (kg/^{m2}), median (range)	28.5 (21-42)
American Society of Anesthesiologists Grade, n (%)	
I	1 (4.7)
II	14 (66.6)
III	6 (28.5)
Site of Rectal Cancer, n (%)	
Lower third	3 (14.2)
Middle third	9 (42.8)
Upper third	5 (23.8)
Recto sigmoid	4 (19.0)
Preoperative Treatment, n (%)	
None	11 (52.4)
Long-course chemo radiotherapy	7 (33.3)
Short-course radiotherapy	3 (14.3)

Tab. 2. Operative and early postoperative data

	Patients (n=21)
Procedure, n (%)	
Anterior resection	16 (81.0)
Abdominoperineal resection	5 (23.8)
Adjacent Visceral Resection, n (%)	
Uterus	4 (19)
Ovary	7 (33.3)
Vagina	2 (9.5)
Prostate	2 (9.5)
Seminal vesicles	6 (28.5)
Urinary bladder	3 (14.2)
Small bowel	4 (19)
Permanent stoma, n (%)	5 (23.8)
Diverting Stoma, n (%)	
Yes	13 (61.9)
No	3 (14.2)
Duration of Robotic Surgery (min), Median (range)	
Operating time	280 (240-430)
Docking time	10 (8-17)
Console time	240 (190-325)
Blood loss (ml), median (range)	20 (0-200)
Postoperative hospital stay (days), median (range)	6 (4-25)
Postoperative ITU admission, n (%)	2 (9.5)
Readmission, n (%)	3 (14.2)

The median hospital course of stay was 6 days (range 4-25), with 2 patients requiring ITU admission after the operation. In the postoperative follow-up period, there were 3 re-admissions mainly due to nausea and vomiting, high output from stoma and poorly controlled pain. The mean per-operative loss of blood was 20 ml (range 5-200), and the mean operative duration was 280 min (range 240-430). We achieved R0 resection in 19 out of 21 patients (Table 3). One positive margin patient had local recurrence during the follow-up period, while the other remained disease-free at the 21-months follow-up. Both patients with R_1 resection received neo-adjuvant long course chemoradiotherapy. Our 90-day mortality was zero; postoperative complications are shown in table 4. With a median follow-up of 36 months, the overall survival at 3 years was 96% and the disease-free survival was 84% (Figure 5). All recurrences occurred within 18 months after surgery.

Tab. 3. Pathological outcomes

	Patients (n=21)
Histological Grading n (%)	
pT4b	8 (38)
pT4a	5 (23)
pT3	8 (38)
Residual Tumor Classification n (%)	
R_0	19 (90.5)
R_1	2 (9.5)
R_2	0
Histological Grade of Resection n (%)	
Grade I	20
Grade II	1
Grade III	0
Number of Lymph Nodes Harvested	
median (range)	20 (9-39)
Lymph Node Metastasis n (%)	
Positive	7 (33.3)
Negative	14 (66.6)

Tab. 4. Morbidity and mortality

	Patients (n=21)
90-Day Mortality, n (%)	
Morbidity n (%)	
Ileus	3 (14.2)
Intraabdominal abscess	4 (19.0)
Anastomotic leakage	1 (4.7)
Stoma problems	1 (4.7)
Surgical site infection	4 (19.3)
Urinary tract infection	4 (19.3)
Pulmonary complications	2 (9.5)
Recurrence, n (%)	
Local	1 * (4.7)
Distant	2 † (9.5)

*R1 Resection; †Liver Metastasis

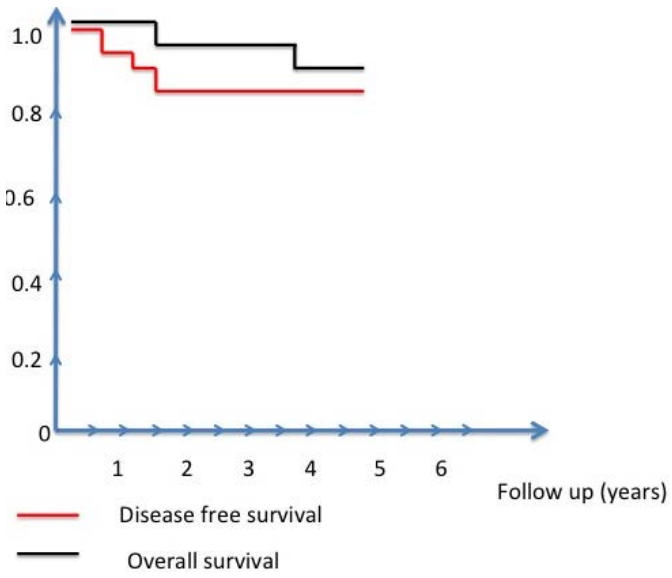

Fig. 5. Disease free and overall survival for patients with locally advanced rectal cancers

DISCUSSION

The laparotomy still considers as the standard procedure for stage T4 rectal carcinoma, and the laparoscopic resection may result in incomplete resection and incomplete TME [13]. Due to technical difficulties, the adoption of laparoscopy in locally advanced rectal cancer remains limited. In patients requiring pelvic exenteration, a laparoscopic vesico-urethral anastomosis or ileal conduit formation is technically demanding. Robotic platforms not only can make these challenging steps relatively easier but also can overcome many of the other limitations of laparoscopy mentioned earlier. In the current literature, there is limited experience about robotic assisted T4 rectal cancer resections.

Intraoperative differentiation of malignant infiltration from inflammatory adhesion is difficult; confirmation can only be made by histopathological examination. Hence, the standard operative strategy for locally-advanced colorectal cancers abutting other vis-cera is to perform en-bloc multi-visceral resection to achieve R0 resection margin. Achieving a clear resection margin reduces the local recurrence risks. Conversely, the rate of local recurrence can be high when an attempt is made to dissect the adherent viscera, as reported in literature [14]. In addition, the 5-year survival is lowered in cases of inadvertent dissection or tumor rupture after en-bloc resections [15]. In our case series, we achieved R0 resec-tion in 90% of cases with locally advanced T4 tumors.

In this series, the malignant infiltration was histologically confirmed in 65% of rectal cancers, which were found adherent to ad-jacent viscera. Nishikawa et al reported 60.9% malignant infiltra-tion to adjacent viscera in a series consisting of open, laparoscopic, and robotic resections, whereas other studies reported 25%-40% malignant infiltration [2,16-18]. A clear resection margin (R0) is one of the most important prognostic factors in the management of stage T4 carcinomas of colorectum [19]. However, even enbloc multi-visceral resection fails to guarantee clear resection mar-gin, varying between 40-90% [2,20-22]. With a higher percentage of R0 resections in our series of robotically-treated patients, we expect better survival outcomes.

There is increased risk of morbidity and mortality with enbloc multivisceral resections for stage T4 rectal carcinomas. Previous studies reported very high morbidity (28%-43%) and mortality rates with open and laparoscopic approach (>13%) [18,22-25]. Using the robotic system, we had no 90-day mortalities, and relatively low morbidity rates (Table 4). This reflects the careful selec-tion of cases after discussion in the MDT meeting, the experience of the principal operating surgeon, experienced trainee fellows, and well-trained operation theater and intensive care unit staff. Furthermore, to achieve low risk of anastomotic leaks and reop-eration rates in these cases, we used triple assessment of colorectal anastomosis, the so-called Portsmouth protocol; this protocol consists of indigo-cyanine green (ICG) in combination with Fire-fly technology (DaVinci), flexible sigmoidoscopy and underwater-leak test [26]. Intra-operative blood loss is usually significant in pelvic exenterative surgery. In our study the reported blood loss ranged from 5 to 300 ml hence this translates in less physiological derangements for patients. The benefit of the robotic platform has also demonstrated a reduced length of stay.

The other benefit of the robotic platform in these patients is the ability to offer a dual console and allow the second surgeon to take active part in the operation and this can minimize the effects of surgical fatigue due to long hours of concentration. As opposed to open pelvic exenteration where there are limited views for the team other than the primary surgeon, the robotic platform offers equal and excellent 3D views to both surgeons adding a further element of safety. Endowrist instruments and a stable camera can provide the surgeon with optimum resources to perform the complex procedures of resecting the prostate, bladder, and seminal vesicles en bloc with the rectal primary.

Selection of patients for minimally invasive procedures is the key for successful surgery in patients with stage T4 carcinomas of rectum. A good radiological report and review of scans with the radiologist at complex cancer MDT is of paramount importance. Centrally based tumors are more favorable for this approach and have a higher R0 resection rate as compared to the lateral or posteriorly based lesions. Experience of the surgical team is another important factor in this context. The learning curve in robotic colorectal surgery was reported, using cumulative sum (CUSUM) method, as being 15-25 cases, with 3 phases of learning; the third phase of mastery can be achieved after 25 cases, when a surgeon can take more advanced cases [27]. Another study by Sng et al [28]

reported this figure to be as higher as 35 cases. We started attempting locally advanced cancers after having performed 100 robotic standard colorectal cancer cases. We do not recommend surgeons attempting locally advanced rectal cancer cases during their initial phase of learning robotic surgery. The lack of tactile feedback can be a major problem in a narrow pelvic cavity and hence only surgeons who are on mastery level should attempt these cases.

Our study describes early experience of robotic en-bloc resections of locally-advanced rectal tumors and is not without limitations. First, the study is single-center, with low patients' volume. Second, the follow-up time is short to make any final comment on survival benefits. A multi-centric collaborative study with longer follow up may provide more evidence in this context. However, all three recurrences in this study were seen in the first 18 months after surgery.

CONCLUSION

The robotic en-bloc resection of adjacent involved multiple visceras for stage T4 rectal carcinoma is technically safe and feasible, with acceptable morbidity and mortality rates. Based on careful patient selection and appropriate robotic experience, this minimally invasive approach can represent an alternative treatment for selected T4 rectal cancers.

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